AMENDMENTS TO THE CLAIMS

1. (Currently Amended): A ~~murine~~ mouse targeting construct comprising:
   (a) a first polynucleotide sequence homologous to a target gene, wherein the target gene is a cGMP phosphodiesterase alpha subunit gene;
   (b) a second polynucleotide sequence homologous to the target gene; and
   (b) a selectable marker.
2. (Original): The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. (Previously Amended): A method of producing a mouse ~~murine~~ targeting construct, the method comprising:
   (a) obtaining a first polynucleotide sequence homologous to a cGMP phosphodiesterase alpha subunit gene;
   (b) obtaining a second polynucleotide sequence homologous to a cGMP phosphodiesterase alpha subunit gene;
   (c) providing a vector comprising a selectable marker; and
   (d) inserting the first and second sequences into the vector, to produce the targeting construct.
4. (Previously Amended): A method of producing a mouse ~~murine~~ targeting construct, the method comprising:
   (a) providing a polynucleotide sequence homologous to a cGMP phosphodiesterase alpha subunit gene;
   (b) generating two different fragments of the polynucleotide sequence;
   (c) providing a vector having a gene encoding a selectable marker; and
   (d) inserting the two different fragments into the vector to form the targeting construct.
5. (Previously Amended): A mouse ~~murine~~ embryonic stem cell comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene.

Claims 6-7. (Canceled)

8. (Previously Amended): A transgenic mouse comprising a homozygous disruption in a cGMP

phosphodiesterase alpha subunit gene wherein said mouse exhibits a phenotype comprising an eye abnormality.

9. (Currently Amended): A cell ~~derived~~ obtained from the mouse of claim 8.

10. (Currently Amended): A method of producing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, the method comprising:

(a) introducing the targeting construct of claim 1 into an embryonic stem cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse, wherein the transgenic mouse comprises a phenotype comprising an eye abnormality or hyperactive behavior.

11. (Currently Amended): A method of identifying an agent that ameliorates an abnormality associated with a homozygous disruption in ~~modulates the expression of~~ a cGMP phosphodiesterase gene, the method comprising:

(a) providing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the mouse exhibits a phenotype comprising an eye abnormality; and

(b) administering an agent to the transgenic mouse; and

(c) determining whether the abnormality ~~expression of cGMP phosphodiesterase in~~ of the transgenic mouse is ~~modulated~~ameliorated.

12. (Currently Amended): A method of identifying an agent that ~~modulates the function of~~ ameliorates an abnormality associated with a homozygous disruption in a cGMP phosphodiesterase gene, the method comprising:

(a) providing ~~a~~ the transgenic mouse of claim 8~~comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene~~;

(b) administering an agent to the transgenic mouse; and

(c) determining whether the ~~function~~ abnormality of the ~~disrupted cGMP phosphodiesterase gene in the~~ transgenic mouse is ameliorated~~modulated~~..

Claim 13-16. (Canceled)

17. (Previously Amended): The transgenic mouse of claim 8, wherein the eye abnormality is a

retinal abnormality.

18. (Previously Amended): The transgenic mouse of claim 17, wherein the retinal abnormality is characterized by retinal degeneration or retinal dysplasia.

19. (Previously Amended): The transgenic mouse of claim 18, wherein the transgenic mouse exhibits an absence of photoreceptor layers.

20. (Currently Amended): The transgenic mouse of claim ~~18~~, wherein the eye abnormality is consistent with vision problems or blindness.

21. (Previously Amended): The transgenic mouse of claim 18, wherein the retinal abnormality is consistent with retinitis pigmentosa.

22. (Currently Amended): The transgenic mouse of claim ~~17~~8, wherein the eye abnormality comprises at least one of the following: thinning or vacuolation of the inner nuclear layer of the eye; thinning of the inner plexiform layer of the eye; loss of ganglion cell nuclei; gliosis of the nerve fiber layer; or attenuation of retinal vasculature.

23. (Currently Amended): A method of producing a transgenic mouse comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse comprises an eye abnormality phenotype, the method comprising:

(a) introducing a cGMP phosphodiesterase alpha subunit gene targeting construct into an embryonic stem cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase gene.

Claims 24-26. (Canceled)

27. (Currently Amended): A method of identifying an agent that ameliorates an eye abnormality, the method comprising:

(a) administering an agent to ~~a~~ the transgenic mouse ~~comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene~~of claim 8;~~;~~ and

(b) determining whether the agent ameliorates the eye abnormality of the transgenic mouse.

28. (Previously Amended): The method of claim 27, wherein the eye abnormality is a retinal

abnormality.

29. (Previously Amended): The method of claim 28, wherein the retinal abnormality is characterized by retinal degeneration or retinal dysplasia.

30. (Previously Amended): The method of claim 29, wherein the transgenic mouse exhibits an absence of photoreceptor layers.

31. (Previously Amended): The method of claim 27, wherein the eye abnormality comprises at least one of the following: thinning or vacuolation of the inner nuclear layer of the eye; thinning of the inner plexiform layer of the eye; loss of ganglion cell nuclei in the eye; gliosis of the nerve fiber layer of the eye; or attenuation of retinal vasculature in the eye.

32. (Currently Amended): A method of identifying an agent which ameliorates an abnormality associated with a disruption of ~~modulates~~ cGMP phosphodiesterase expression, the method comprising:

(a) administering an agent to ~~a~~ the transgenic mouse of claim 8~~comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse comprises a phenotype comprising an eye abnormality~~; and

(b) determining whether the agent ~~modulates cGMP phosphodiesterase expression~~ ameliorates the phenotype in the transgenic mouse, wherein ~~a modulation~~ amelioration of the phenotype is indicative of an agent which ameliorates an abnormality associated with a disruption ~~a modulation~~ of cGMP phosphodiesterase expression.

33. (Currently Amended) A method of identifying an agent which modulates a phenotype comprising an eye abnormality, wherein the phenotype is associated with a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene, the method comprising:

(a) administering an agent to ~~a~~ the transgenic mouse of claim 8 ~~comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene~~; and

(b) determining whether the agent modulates the phenotype.

Claim 34. (Canceled)

35. (Currently Amended): A method of identifying an agent which modulates a phenotype associated with a disruption in an cGMP phosphodiesterase alpha subunit gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a homozygous

disruption in an cGMP phosphodiesterase alpha subunit gene, wherein said mouse exhibits an eye abnormality or hyperactivity; and

(b) determining whether the agent modulates the phenotype.

Claims 36-41. (Canceled)

42. (Previously Amended): A transgenic mouse comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene, wherein the transgenic mouse exhibits a phenotype comprising hyperactive behavior.

Claims 43-44. (Canceled)

45. (Currently Amended): A method of identifying an agent that ameliorates hyperactive behavior, the method comprising:

(a) administering an agent to ~~a~~ the transgenic mouse of claim 42~~comprising a homozygous disruption in an cGMP phosphodiesterase alpha subunit gene~~; and

(b) determining whether the agent ameliorates hyperactive behavior of the transgenic mouse.

Claim 46. (Canceled)

47. (Currently Amended): A method of identifying an agent which modulates a phenotype associated with a disruption in a cGMP phosphodiesterase gene, the method comprising:

(a) administering an agent to ~~a~~ the transgenic mouse of claim 42~~comprising a homozygous disruption in a cGMP phosphodiesterase alpha subunit gene~~; and

(b) determining whether the agent modulates hyperactive behavior of the transgenic mouse.

Claim 48. (Canceled)